REMARKS

Reconsideration and withdrawal of the rejections of the pending claims are respectfully requested in view of the amendments and remarks herein, which place the application in condition for allowance.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 1-11 are under consideration in this application. Claim 1 has been amended for clarity. Claims 1, 2, 5, and 7 have been amended to comply with the proper Markush claim language. Claim 10 has been amended to define the claim dependency. No new matter has been added.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited in the Office Action, and that these claims were in full compliance with the requirements of 35 U.S.C. § 112. It is submitted that the amendments of the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled.

The issues raised by the Examiner in the Office Action are addressed below in the order they appear in the prior Action.

II. THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, IS OVERCOME

Claim 2 is rejected under 35 U.S.C. § 112, second paragraph as allegedly having an insufficient antecedent basis for the limitation "the glycol ethers". Applicants respectfully disagree.

The Examiner contends that claim 2 recites the limitation "glycol ethers" in claim 1 and that there is insufficient antecedent basis for this limitation in the claim. Applicants respectfully traverse. Claim 2 as amended recites that co-solvent selected from the group consisting of glycol ethers is additionally included in the formulation of claim 1. Therefore, Applicants believe that the rejection is improper.

The Examiner further requests that proper Markush group language should be used (i.e. "a solvent selected from the group consisting of glycol ethers'). Claim 2 has been amended according to the Examiner's request thereby obviating the rejection.

In view of the above, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph, are respectfully requested.

III. THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, IS OVERCOME

Claims 1-11 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as invention.

The Examiner contends that claims 1-11 are vague and indefinite because of the use of the term "comprising" in Markush language set up.

Although applicants do not agree with the rejection, in the interest of expediting prosecution, claims 1, 2, 5, and 7 have been amended to comply with the Markush group language indicated by the Examiner, thereby obviating the rejection.

Therefore, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph, are respectfully requested.

IV. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, IS OVERCOME

Claim 11 is rejected under 35 U.S.C. § 112, first paragraph, as allegedly providing no reasonable enablement for the prevention of infection of cattle with *Cooperia* or *Ostertagia*, while being enabling for a method of treating infections of cattle with *Cooperia* or *Ostertagia* through the administration of the formulation.

According to the Court of Appeals for the Federal Circuit in the case of *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988),

> Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. 'The key word is undue, not

> experimentation.' The determination of what constitutes undue experimentation in a given case requires the application of standard of reasonableness, having due regard for the nature of the invention and the state of the art. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed ... [Citations omitted]. *Id.* at 1404.

Determining whether undue experimentation is required to practice a claimed invention turns on weighing many factors summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), for example: (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples of the invention; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims.

Thus, it is respectfully submitted that for a proper Section 112, first paragraph, lack of enablement analysis, an Office Action must show that the Wands factors are not met. Simply, it is respectfully asserted that the lack of enablement rejection fails to provide a fact based analysis using the Wands factors that supports the proposition the claimed invention require undue experimentation.

The Office Action contends that the specification does not enable one skilled in the art to practice the invention commensurate in scope with the claims. The Office Action further asserts that there is a lack of scientific data and working embodiments regarding prevention of parasitic infection, and that one skilled in the art would be required to conduct an undue amount of experimentation to determine how to prevent parasitic infection in cattle by administering Applicant's formulation. The Examiner further alleges that the strategies for preventing parasitic infections are not available by reciting a paragraph from the Merck Manual.

The Examiner is respectfully reminded that a specification need not contain any example of the invention, as the issue is whether the disclosure enables one skilled in the art to practice the invention without undue experimentation. *In re Borkowski*, 422 F.2d 904, 164 USPQ 642

(CCPA 1970). Simply, a determination that undue experimentation is necessary to practice the invention does not necessarily follow from a lack of examples in the specification. And, the Examiner is further respectfully reminded that an applicant need not describe all actual embodiments of a claimed invention.

The present invention relates to the prevention of infection of cattle with Cooperia or Ostertagia through the administration of the claimed formulation. Based upon the teachings of the specification, one of skill in the art could extrapolate the dosage for treating infection of cattle with *Cooperia* or *Ostertagia* to preventing infection of cattle with *Cooperia* or *Ostertagia* without undue experimentation.

Contrary to the Examiner's assertion, the recited paragraph from the Merck Manual relates to the parasitic infections in humans and not in cattle. The use of anthelmintic drugs for prevention of parasitic infections in cattle is a known practice for one skilled in the art. The Merck Veterinary Manual relates to such strategies in several chapters related to parasitic infections caused by nematodes. In "General Control Measures", the Manual states that "strategic use of anthelmintics is designed to reduce worm burdens and thereby, the contamination of pastures". It also recites that "timing of administration is based on knowledge of the seasonal changes in infection and the regional epidemiology of the various helminthoses" and that current practices "indicate the effectiveness of 2 or more anthelmintic treatments (usually at intervals of 3-5 wk) given when cattle first go to grass in spring" (www.merckvetmannual.com/mvm/htm/bc/22400.htm). A supplemental IDS citing the Merck Veterinary Manual is being submitted concurrently with this response. As such, one skilled in the art would be able to use the claimed formulation for prevention of the disclosed parasitic infections based on the commonly accepted prevention practices.

Therefore, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph, are respectfully requested.

V. THE REJECTION UNDER 35 U.S.C. §102 IS OVERCOME

Claims 1, 3-5, and 7-10 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Komer *et al.* (U.S. Patent No. 5,773,422). Applicants respectfully traverse the rejection.

It is respectfully pointed out that a two-prong inquiry must be satisfied in order for a Section 102 rejection to stand. First, the prior art reference must contain all of the elements of the claimed invention. *See Lewmar Marine Inc. v. Barient Inc.,* 3 U.S.P.Q.2d 1766 (Fed. Cir. 1987). Second, the prior art must contain an enabling disclosure. *See Chester v. Miller,* 15 U.S.P.Q.2d 1333, 1336 (Fed. Cir. 1990). A reference contains an enabling disclosure if a person of ordinary skill in the art could have combined the description of the invention in the prior art reference with his own knowledge of the art to have placed himself in possession of the invention. *See In re Donohue*, 226, U.S.P.Q. 619, 621 (Fed. Cir. 1985).

The Examiner alleges that Komer discloses novel formulations for the administration of avermectin dissolved in N-methylpyrrolidone or 2-pyrrolidone or mixtures thereof and therefore addresses the limitations recited in instant claims 1 and 3.

Contrary to the Examiner's assertions, Komer does not anticipate the present invention. Claim 1, as amended, recites: "A stable formulation suitable for administration to animals comprising at least one active selected from the group consisiting of avermectins and milbemycins and levamisole and **both** of said actives being dissolved in a pyrrolidone solvent". Therefore, the claimed formulation requires at least two actives, wherein at least one is selected from avermectins and milbemycins and the other one is levamisole. The claimed formulation requires at least two actives belonging to two structurally different classes of compounds. Levamisole, is another active ingredient in the claimed formulation in addition to at least one avermectin or milbemycin. Levamisole is an antibiotic belonging to a class of synthetic imidazothiazole derivatives structurally unrelated to macrocyclic lactones, such as avermectins and milbemycins. Komer does not teach or suggest the use of levamisole in the described formulations. Moreover, Komer does not relate to the use of milbemycin in the disclosed formulations. As such, Komer does not teach or suggest all the elements of the pending claims and therefore does not anticipate the present invention.

Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) are respectfully requested.

VI. THE REJECTIONS UNDER 35 U.S.C. § 103(a) ARE OVERCOME

Claims 1and 2 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Komer (U.S. Patent No. 5,773,422) in view of Huet *et al.* (U.S. Patent No. 6,426,333) and Harvey (U.S. Patent No. 6,165,987). Applicants respectfully disagree and traverse the rejection.

The Examiner is respectfully reminded of the case law, namely, that there must be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); *In re Obukowitz*, 27 U.S.P.Q. 2d 1063 (BOPAI 1993). As stated by the Court in *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992): "The mere fact that the prior art may be modified in the manner suggested by the Office Action does not make the modification obvious unless the prior art suggests the desirability of the modification." Also, the Examiner is respectfully reminded that for the Section 103 rejection to be proper, both the suggestion of the claimed invention and the expectation of success must be founded in the prior art, and not Applicants' disclosure. *In re Dow*, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988).

Furthermore, the Supreme Court has recently reaffirmed the factors set out in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18: "[T]he scope and content of the prior art are determined; differences between the prior art and the claims at issue are...ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented." *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727.

Applying the law to the instant facts, the references relied upon by the Office Action do not disclose, suggest or enable Applicants' invention. The cited references do not teach or suggest the presently claimed invention as none of them relates to the formulations comprising levamisole in combination with avermectins or milbemycins to overcome parasite resistance, particularly in *Cooperia* or *Ostertagia* parasite species.

The Office Action alleges that it would have been *prima facie* obvious to an ordinary skilled artisan at the time the instant invention was made to modify the formulation of Komer by incorporating additional solvents like glycol ethers as taught by Huet *et al.*, because Harvey discloses that the anthelmintic agents need to be administered as solutions by dissolving them in solvents such as ethers to be bioavalable.

Applicants respectfully submit that establishing a *prima facie* case of obviousness requires that the prior art reference must teach or suggest all the claim limitations.

None of the references cited on the Office Action teach or suggest the use of levamisole in combination with avermectins or milbemycins. There is no teaching or motivation in Komer to use levamisole in the described formulations. Komer does not relate to levamisole as a an additional active in the formulations for treating pesticidal infections, providing no motivation to modify the described formulations to further include levamisole and showing no expectation of success of such formulations as disclosed in the pending claims.

Huet *et al.* relates to the use of 1-phenylpyrazoles in combination with macrocyclic lactone anthelmintic agents and does not teach or suggest the use of levamisole in such formulations.

Harvey relates to the use of praziquantel in combination with macrocyclic lactone anthelmintic agents and does not teach or suggest the use of levamisole in such formulations.

Claims 1 and 6 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Komer (U.S. Patent No. 5,773,422) in view of Harvey (GB Patent Application No. 2252730). Applicants respectfully traverse the rejection.

The Office Action further rejects claims 1 and 6 as obvious over Komer in view of Harvey, as allegedly teaching the formulations comprising levamisole in an amount of 1-30% w/v.

Applicants respectfully submit that Harvey relates to levamisole hydrochloride as a possible additional anthelmintic agent to be used in combination with praziquatel (page 2 of the specification as published) and not with avermectins or milbemycins as disclosed in the pending claims. Furthermore, Harvey relates to formulations comprising levamisole in an amount of 1-10% w/v (page 3 of the specification as published) and does not teach or suggest the use of pyrrolidone solvent in formulations comprising levamisole. Therefore, based on the cited references, it would not be obvious to one skilled in the art that combining levamisole with at least one avermectin or milbemycin would produce a stable formulation in pyrrolidone solvent.

Claims 1 and 11 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Komer (U.S. Patent No. 5,773,422) in view of Harvey (U.S. Patent No. 6,165,987). Applicants respectfully disagree.

The Office Action further asserts that based on the reference by Komer in view of Harvey, claims 1 and 11 are *prima facie* obvious as one skilled in the art would modify the method of Komer via treating parasitic infection caused by *Cooperia* or *Ostertagia* as taught by Harvey. The Office Action contends that a skilled artisan would have a reasonable expectation of success upon combination of the prior art teachings because both Komer and Harvey teach within the same field of endeavor and address the same problem, namely the treatment of parasitic infections, which are caused by the parasitic species like *Cooperia* or *Ostertagia*.

Contrary to the Examiner's assertion, one skilled in the art would not have a reasonable expectation of success upon combination of the prior art teachings, as none of the cited references addresses the difficulties of preparation of the claimed formulation and its stability in a non-aqueous solvent system.

It was previously found that differing pH requirements of levamisole and other anthelmintics made it difficult to formulate a stable product (page 1, paragraphs 0016-0018 of the specification as published). The present formulation excludes water, the issue of incompatible pH requirements, enabling the two actives to coexist in a stable single phase. The cited references do not relate to the preparations of such formulations. Moreover, Komer and Harvey relate to formulations that allow water as a solvent and therefore are teaching away from the present invention.

Furthermore, it has been shown that the claimed combination of actives exhibited outstanding efficacy against all parasite species (p. 8, paragraphs 0107-0110 of the specification as published) and successfully resolved the problem of anthelmintic resistance. None of the references cited in the Office Action relates to the solution presented by the present invention.

As claimed, the invention provides a stable formulation that can successfully treat the infections caused by all parasite species, in particular by Cooperia, which is the key dose limiting parasite of the avermectin/milbemycin group and Ostertagia, which is a limiting parasite of levamisole, by combining the effective amounts of at least one avermectin or milbemycin and levamisole in a pyrrolidone solvent.

As such, the cited references do not render the pending claims *prima facie* obvious. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. § 103(a) are respectfully requested.